· 综述 ·

心房颤动导管消融术的创新和策略转变

赵海娟 李珂 赵耀 黄松群 郭志福
(海军军医大学第一附属医院心血管内科,上海 200433)

【摘要】心房颤动的治疗在过去几十年中发生了巨大的变化,尤其是在非药物治疗方面取得了重要进展,导管消融术正逐步成为心房颤动患者的一线治疗方案。肺静脉隔离是导管消融的基石,但由于肺静脉隔离不完全和其他非肺静脉触发灶等因素,通常需再次行导管消融术,因此还需进一步开发消融设备,改进消融策略。现概述心房颤动导管消融术的发展,介绍最新技术以及临床研究和未来发展方向。

【关键词】心房颤动;肺静脉隔离;导管消融;心房颤动复发
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Innovations and Paradigm Shifts in Atrial Fibrillation Ablation

ZHAO Haijuan, LI Ke, ZHAO Yao, HUANG Songqun, GUO Zhifu
(*Department of Cardiology*, *The First Affiliated Hospital of Naval Medical University*, *Shanghai* 200433, *China*)

【Abstract】Treatment of atrial fibrillation has seen dramatic breakthroughs in the past decades, especially in the field of non-pharmacological treatment. In order to have a better rhythm control, catheter ablation has gradually become the first-line therapy for patients with atrial fibrillation. Pulmonary vein isolation is the cornerstone of catheter ablation. However, re-do procedures are often necessary due to incomplete pulmonary vein isolation and non-pulmonary vein triggers. Therefore, there is further need for developing ablation tools and strategies that reproducibly isolate the pulmonary vein transmurally. In this review, we will summarize the development of catheter ablation in atrial fibrillation, and introduce the latest technologies, clinical researches and future endeavours.

【Key words】Atrial fibrillation; Pulmonary vein isolation; Catheter ablation; Atrial fibrillation recurrence

心房颤动(房颤)是最常见的持续性心律失常,以其高发病率和高死亡率引起广泛关注。肺静脉隔离(pulmonary vein isolation, PVI),尤其对于阵发性房颤患者来说,逐渐成为维持窦性心律和改善症状的首选治疗方法[1],但仍有 10% ~35% 的复发率[2]。PVI 术后房颤复发的原因复杂,首先在目前消融模式下消融灶有时不能获得永久性透壁损伤,因此消融点会恢复电传导[3]。其次许多房颤患者合并基础心血管疾病,如高血压、心力衰竭和瓣膜疾病,通常会有明显的心房扩大和心房纤维化,肺静脉外触发灶明显增多[4]。因此,有必要进一步研发可安全高效行 PVI 的消融设备,以及根据房颤患者的临床特征制定个性化的消融方式与策略。

1 导管消融技术

1998 年 Haïssaguerre 等[5]描述了心房肌延伸至肺静脉产生的局灶激动对于房颤触发的作用,奠定了目前房颤心内膜和心外膜消融策略的基础,标志着导管消融治疗房颤新时代的开始。PVI 是房颤导管消融治疗的基石,近年来随着技术的不断进步,用于 PVI 的导管也在不断改进和创新。

1.1 逐点消融技术

目前使用最广泛的消融方法是使用经皮导管逐点射频消融肺静脉[6]。通过导管尖端输送射频电流,高阻抗的心肌消耗电能产生热能,引起组织破坏,造成局部损伤。逐点射频消融肺静脉,组成隔离带,其损伤范围均匀可控,边界清楚。而高功率输出或消融温度过高将导致不良事件的发生,如爆破、血栓形成、消融局部表面形成焦痂等,盐水灌注消融导管的研发有效提高了逐点射频消融的安全性和效率。近年来压力监测射频消融导管进一步引入了阻抗信息、组织贴靠力、导管稳定性、消融时间和导管尖端温度控制等参数[7],增加消融的安全性,缩短消融时间,减少透视需求。为进一步推进逐点射频消融的治疗效果,有

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通信作者:郭志福,E-mail:guozhifu@126.com

研究[8]证明高功率短时程(50 W 消融 10 s)的逐点射频消融方法与低功率长时程(25 ~ 35 W 消融 60 s)方法的安全性、有效性相当,且能缩短手术时间。更高功率和更短时程的消融方式也已在进行当中,其效果仍需大型临床试验进行证明。

1.2　单次激发技术

单次激发消融技术在过去的十几年里也得到了发展,这种方法的优点在于一次消融就能隔离肺静脉,而不必逐点隔离,可显著缩短消融时间和术者的学习曲线。广泛使用的单次消融设备有低温冷冻球囊消融、激光球囊消融,近期兴起的脉冲电场消融(pulse field ablation,PFA)也被证明可用于 PVI,且透壁性更佳,PVI 的持久性更好,见图 1。

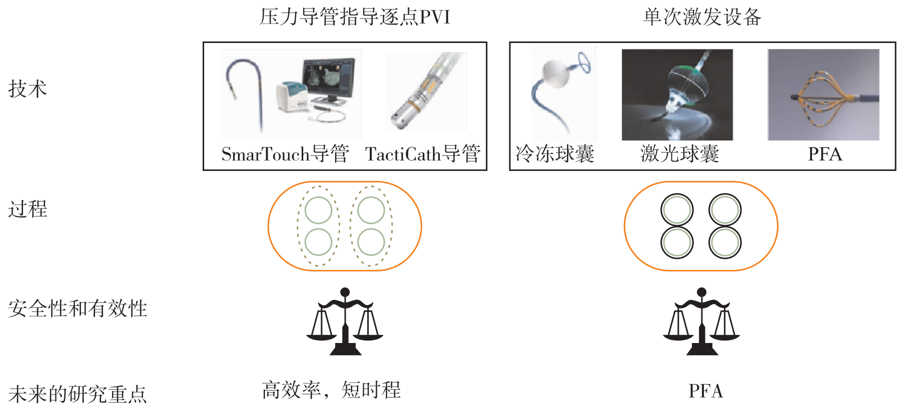

图 1　逐点消融和单次激发设备的现状与未来研究重点

1.2.1　冷冻球囊消融

冷冻球囊消融是将液态制冷剂一氧化二氮(N_2O)由体外导管输送到末端球囊,制冷剂气化形成低温,消融部位温度骤然降低,使局部组织细胞坏死,破坏局灶电位传导,消除房颤。在 FIRE AND ICE 研究[9]中比较了阵发性房颤患者逐点射频消融与冷冻消融的效果,结果表明在多次冷冻消融的患者中肺静脉电位重新连接的机会也更少,只需更少的额外损伤就能成功形成 PVI,患者更易耐受,严重并发症少。

1.2.2　激光球囊消融

激光球囊消融设备由 980 nm 激光二极管和充满氧化氘的顺应性球囊组成,球囊的中心管腔内有内窥镜和可调节光纤,能直接观察到肺静脉组织并产生 30°扇形激光的可见光和近红外光消融(激光)能量,激光能量弧可连续扫射在肺静脉前庭的所需部位,灼烧心肌细胞[10]。一项激光球囊消融与射频消融的随机对照试验[11]中,353 例阵发性房颤患者接受 PVI 治疗,证明了激光球囊消融的有效性不劣于射频消融,同样在持续性房颤中也得到证明[12]。激光球囊消融与冷冻球囊消融相比,术后无房性心律失常复发的比例相似(78% vs 80%),两种消融方式的总透视时间无显著性差异,但冷冻球囊消融手术时间明显缩短[13]。

1.2.3　PFA

在单次激发消融设备领域,PFA 由于其选择性损伤心肌组织的特性,目前备受关注。PFA 通过采用一系列微秒瞬时发放的持续性高振幅电脉冲,在心肌细胞膜上形成不可逆电穿孔,达到非热消融的目的,使房颤导管消融更加安全有效[14-15],与其他消融方式相比,避免了对消融区域临近组织如食管、冠状动脉和膈神经等的非选择性损坏。目前已有多中心研究[16-18]证明,在阵发性或持续性房颤中,PFA 治疗房颤在急性期及短时间随访内是安全可行的。对于这种新型的单次消融设备还需更大规模多中心的长期研究,并与其他单次消融设备或逐点消融方式进行对比。

2　导管消融策略

在过去 20 年里 PVI 在技术方面取得了不错成就,但持续性房颤患者长期成功率仍有限[19]。PVI 的预后除与消融部位的持久性和透壁性有关外,还受到心房基质和心房重塑程度相关因素的影响,如房颤类型、左心房大小和相关基础条件等[20]。对于持续性房颤患者,仅采用 PVI 治疗往往不足以长期维持窦性心律,存在消融术后复发等问题,因此如何降低房颤导管消融术后复发率是一个亟需解决的问题。

2.1　术前患者评估

筛选出适合导管消融治疗的患者,可增加房颤消融的有效性,在过去几年里,临床上引入了几种风险评分来预测房颤复发[21]。APPLE 评分[22]包括年龄、房颤类型、慢性肾功能不全、左心房直径和左室射血分数等基础条件,这些都与单次 PVI 后房颤的复发有关。DR-FLASH 评分[23]与左心房低电压区有关,它作

为房颤基质的测量,已被证明是导管消融术后心律失常复发的一个强有力的预测因素。N 末端脑钠肽前体等生物标志物也被纳入风险评分中,研究[24]证明其能很好地对低电压区域进行预测。此外左心房成像也被用来评估左心房基质,在 DECAAF 研究[25]中所有患者在 PVI 前行左心房延迟增强磁共振成像(magnetic resonance imaging,MRI),发现心房组织纤维化与房颤复发风险增加有关。Khurshid 等[26]证明基于人工智能的 12 导联心电图分析可同房颤临床危险因素模型一样对房颤有相似的预测作用,二者互相补充,有效量化未来房颤风险。通过术前对患者进行充分评估,可筛选出 PVI 术最大获益人群。

2.2　术中消融策略选择

EAST-AFNET 4 研究[27]显示早期节律控制可显著减少不良心血管事件结局。目前临床上最常见的消融策略除 PVI 外还包括解剖消融策略,如线性消融、左心耳隔离、上腔静脉隔离、冠状窦隔离和腔内指导的消融策略,如转子消融、碎裂电位消融、非肺静脉触发灶消融和磁导航指导消融[28]。图 2 提供了一种治疗策略选择的方式,左心房容积越大,房颤负荷越重,有更多基础疾病的患者可联合多种消融策略[20]。

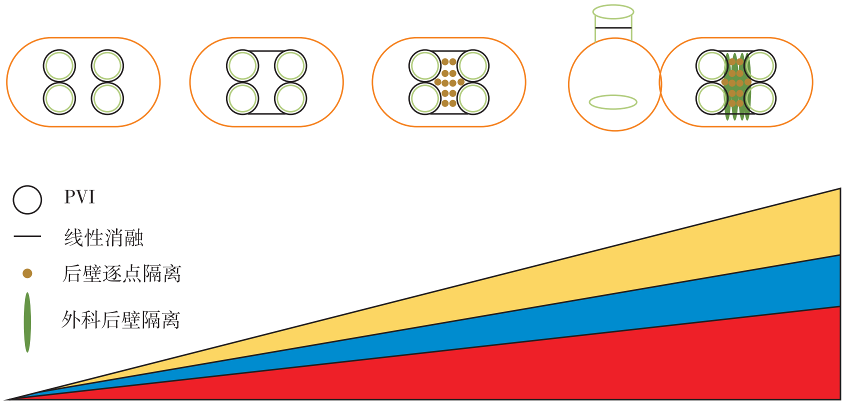

图 2　消融策略与左心房体积、房颤负荷和基础情况的关系

线性消融主要包括左心房顶部线、左心房底部线、二尖瓣峡部线以及三尖瓣峡部线的消融。STAR-AF Ⅱ[29]和 SMAN-PAF 试验[30]比较了 PVI 联合线性消融术与单独 PVI 消融房颤的手术效果,两项试验均发现房颤患者无获益,且增加线性消融导致手术时间延长,但试验中消融技术是否足以造成消融线的透壁性损伤及双相阻滞仍存在疑问。对于一些有较多基础疾病或左心房增大的患者,还能联合胸腔镜手术进行心外膜消融,以形成透壁损伤,提高手术成功率[31]。虽然线性消融在临床中未常规进行,但相信随着导管技术的改进能降低术后心律失常的发生率,并在未来广泛应用。有研究[32]表明 PVI 联合 Marshall 静脉酒精消融与单独 PVI 相比,可增加 12 个月无房颤或房性心动过速的可能性。

MRI 和电压图显示的心房纤维化与房颤的发生和维持有关[33]。Kircher 等[34]证实与传统的根据房颤类型选择线性消融的方法相比,利用电压图指导单独制定房颤基质改良的方法可显著提高无心律失常患者的生存率。与此同时,还能在 MRI 指导下为患者定制最佳消融策略。在一项随机试验[35]中,155 例房颤患者被随机分配到 PVI 组或 PVI 联合纤维化消融组,结果显示 MRI 指导下的 PVI 无改善。DECAAF Ⅱ研究[36]也发现根据纤维化程度指导的消融较单独 PVI 无差异,但治疗后分析发现,对于纤维化程度低(<左心房体积的 20%)的患者其消融有统计学意义。对于不同患者,应首选更有针对性和个性化的消融策略,而不是进行“一刀切”的消融。

2.3　术后抗心律失常药治疗策略

最新国内外指南[37-38]指出导管消融术后使用抗心律失常药(antiarrhythmic drug,AAD)可减少房颤复发。EAST-AF 研究[39]纳入 2 038 例接受射频导管消融的房颤患者,评估术后空白期内应用 AAD 是否可降低早期心律失常复发的发生率,发现 AAD 组较对照组 90 d 内房颤复发率显著降低,AAD 可促进左心房重塑的逆转,改善长期临床结果。POWDER AF 研究[40]也证明行 PVI 术后的阵发性房颤患者持续使用 AAD 在术后 3~12 个月的随访期发生房性快速性心律失常的概率较未使用组显著减少。AAD 治疗目标是改善房颤相关症状,目前术后空白期内最常用的 AAD 是胺碘酮,然而较高的副作用发生率限制了其在临床上的广泛使用。决奈达隆也是Ⅲ类 AAD,它在胺碘酮的基本结构上脱去碘基,引入甲磺酰胺基,保留了胺碘酮抗心律失常的电生理特性,其主要安全终点优于胺碘酮[41]。决奈达隆的安全性目前已在

广泛人群中得到验证,ARTEMIS AF 研究[42]也证实,胺碘酮复律后立即转换为口服决奈达隆的房颤复发率更低。

2.4　术后抗凝治疗策略

目前临床研究[43]已证实导管消融的有效性和安全性,相较于传统的药物治疗,导管消融可更好地维持窦性心律并显著改善症状和生活质量。但导管消融并未成为预防血栓事件的治疗手段[44]。指南[45]建议,对于卒中高危的房颤患者,即使导管消融术后成功转复窦性心律,仍应长期服用抗凝药物。而对于卒中高危的患者,服用传统抗凝药物的出血风险相对较高,故需要一种抗凝替代方案。

90%以上心源性血栓栓子来源于左心耳。因此,左心耳封堵或缝合结扎可成为预防房颤患者血栓事件的替代治疗手段。WATCHMAN、ACP/Amulet、LAmbre 封堵器的数项大规模随机对照试验及前瞻性研究表明,与传统的维生素 K 拮抗剂和新型口服抗凝药物相比,左心耳封堵术预防血栓事件的效果并不逊色,已成为预防房颤血栓栓塞事件的重要替代治疗方式。房颤导管消融与左心耳封堵术具有相同的操作途径,在单次手术中同时完成,可同时满足缓解房颤症状和预防血栓栓塞事件的作用。因此,指南[45]建议对于存在长期抗凝治疗禁忌证且具有高卒中风险的症状性房颤患者,房颤导管消融联合左心耳封堵术可成为治疗选择方案。

3　房颤治疗方式的转变

回顾房颤消融的创新和模式转变,心室率控制与节律控制一直是房颤治疗的重点[37]。节律控制管理的主要目标是减轻房颤症状,最近发表的几项大型随机对照试验证明节律控制较心室率控制更为重要。CABANA 系列研究[46]发现与药物治疗相比,导管消融未显著降低死亡率、致残卒中率、大出血发生率等主要复合终点,但房颤复发率明显降低,并且症状性房颤患者临床生活质量显著改善。可能原因是超过一半的患者患有持续性房颤,房颤负荷重,且由于有较多患者进行交叉治疗,终点事件的发生率远低于预期,削弱了该研究的统计效力。对于心力衰竭合并房颤患者[47],随访 48.5 个月,导管消融组较单纯药物治疗组的主要复合终点、全因死亡率以及房颤复发率均降低;随访 60 个月,导管消融在改善患者临床生活质量上有优势。该研究[48]近期还发现,与药物治疗相比,导管消融术的临床结局存在基于年龄的差异,在年轻患者中导管消融术的相对和绝对益处最大。在年长患者中未观察到消融术的预后益处。在治疗相关并发症或导管消融术预防复发性房性心律失常方面,未发现年龄差异。CASTLE-AF 研究[49]也表明心力衰竭合并房颤患者进行导管消融的全因死亡或心力衰竭恶化住院的发生率显著低于药物治疗。与 CABANA 研究不同,EAST-AFNET 4 研究[50]纳入的是早期房颤(病史 <1 年)患者,随机分为早期节律控制组与常规治疗组,两年后接受早期节律控制的患者出现主要复合结局的风险较低。虽然有关房颤负荷的数据仍在等待中,但试验表明较长的窦性心律与改善预后相关。这些最近的试验结果提示,在疾病过程中进行早期的干预以维持窦性心律对于预后是有好处的。消融在维持窦性心律方面比 AAD 更有效,有望成为一线治疗方案。

4　总结

在过去的 20 年里,PVI 已成为症状性房颤节律控制的标准治疗方式。最近的大型随机对照试验数据表明,PVI 不仅可减轻房颤负荷、改善生活质量,而且还可改善预后。近年来导管消融技术已取得了较大进展,如 PFA。PFA 可"精准"消融,在提升效率的同时,将一定程度上减少传统消融技术带来的并发症。此外,综合性管理以及个体化消融方案,也将有助于提高手术成功率,改善房颤预后。如何降低持续性房颤消融术后复发率,一直是困扰临床工作的大问题,新型消融能量的应用能否解决,有待临床试验进一步观察。

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